

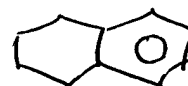
=> d his

(FILE 'HOME' ENTERED AT 09:28:26 ON 06 FEB 2001)

FILE 'REGISTRY' ENTERED AT 09:28:36 ON 06 FEB 2001

L1 STR
L2 50 S L1
L3 STR
L4 STR L3
L5 13 S L1 AND (L3 OR L4)
L6 421495 S C6/ESS AND (OC4/ES OR SC4/ES)
L7 50 S L1 SSS SAM SUB=L6
L8 3870 S L1 AND (L3 OR L4) FUL
L9 155 S L8 AND C6-C6/ES
L10 STR
L11 50 S L10
L12 62880 S 591.49.51/RID
L13 19 S L8 AND L12

Ring identifier for:



19 compounds

FILE 'CAPLUS' ENTERED AT 09:36:59 ON 06 FEB 2001

L14 7 S L13
L15 51 S L9
L16 44 S L15 NOT L14
L17 29 S L16 AND P/DT

7 cites caplus

FILE 'CAOLD' ENTERED AT 09:39:01 ON 06 FEB 2001

L18 0 S L13

FILE 'CAPLUS' ENTERED AT 09:39:11 ON 06 FEB 2001

FILE 'REGISTRY' ENTERED AT 09:41:20 ON 06 FEB 2001

L19 STR L1
L20 STR L3
L21 STR L20
L22 50 S L20 OR L21 SSS SAM SUB=L8
L23 STR L20
L24 STR L21
L25 25 S L23 OR L24 SSS SAM SUB=L8
L26 582 S L23 OR L24 SSS FUL SUB=L8

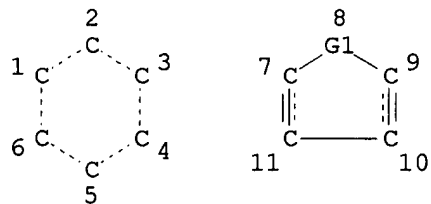
FILE 'CAPLUS' ENTERED AT 09:48:02 ON 06 FEB 2001

L27 133 S L26
L28 35 S L27 AND P/DT

=> d que 18

L1

STR



VAR G1=O/S

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

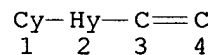
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NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

L3

STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

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GGCAT IS MCY LOQ UNS AT 2

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

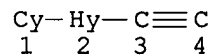
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 4

STEREO ATTRIBUTES: NONE

L4

STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

GGCAT IS UNS AT 1

GGCAT IS MCY LOQ UNS AT 2

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 4

STEREO ATTRIBUTES: NONE

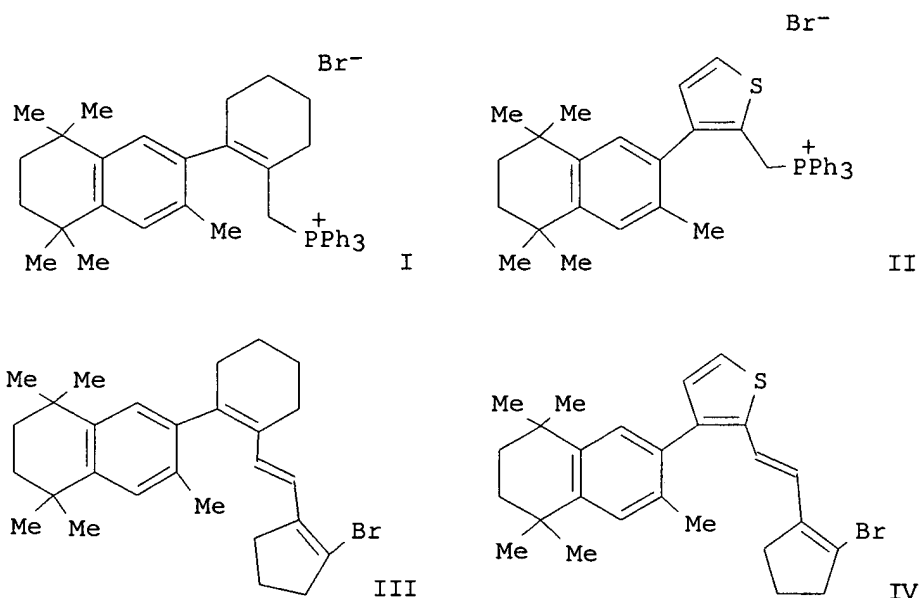
QAZI

09/619584

L8 3870 SEA FILE=REGISTRY SSS FUL L1 AND (L3 OR L4)

=> d bib abs hitstr 114 1-7

L14 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2001 ACS
 AN 2000:26526 CAPLUS
 DN 132:222673
 TI Preparation of 9,13-di-cis double bond locked retinoids
 AU Qing, Feng-Ling; Yue, Xiang-Jun
 CS Shanghai Inst. Organic Chem., Chin. Acad. Sci., Shanghai, 200032, Peop. Rep. China
 SO Chin. J. Chem. (2000), 18(1), 76-84
 CODEN: CJOCEV; ISSN: 1001-604X
 PB Science Press
 DT Journal
 LA English
 OS CASREACT 132:222673
 GI



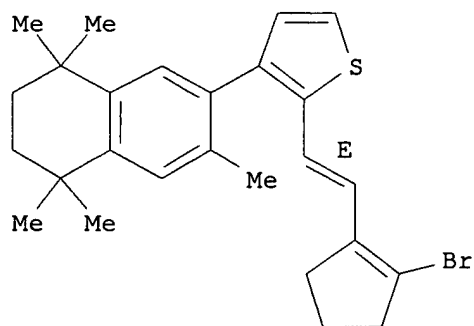
AB Synthesis of two retinoids where the 9,13-di-cis double bonds were locked in cycloalkene or thiophene was accomplished. The key steps were the Wittig olefination of phosphonium salt I and II with 2-bromocyclopentenecarboxaldehyde, followed by carbonylation of vinyl bromide III and IV with carbon monoxide in the presence of $\text{Pd}(\text{PPh}_3)_4$.

IT **199529-75-4P 199529-76-5P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of 9,13-di-cis double bond locked retinoids)

RN 199529-75-4 CAPLUS

CN Thiophene, 2-[(1E)-2-(2-bromo-1-cyclopenten-1-yl)ethenyl]-3-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)- (9CI) (CA INDEX NAME)

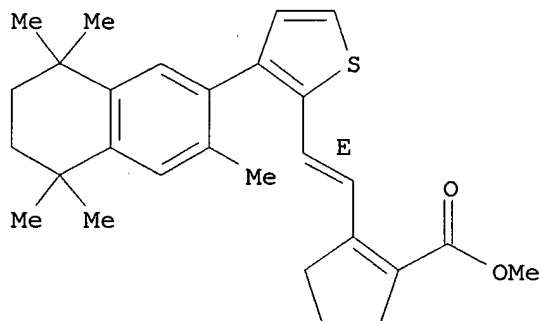
Double bond geometry as shown.



RN 199529-76-5 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[(1E)-2-[3-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)-2-thienyl]ethenyl]-, methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT 199529-63-0P

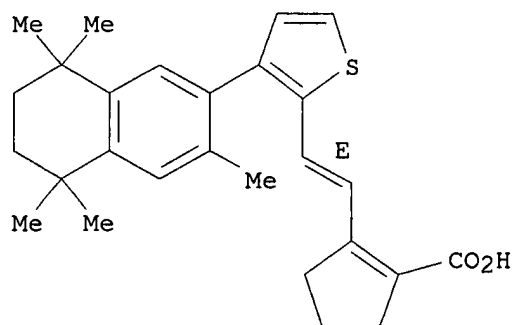
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 9,13-di-cis double bond locked retinoids)

RN 199529-63-0 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[(1E)-2-[3-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)-2-thienyl]ethenyl]- (9CI) (CA

INDEX
NAME)

Double bond geometry as shown.



RE.CNT 23

RE

- (1) Allenby, G; Proc Natl Acad Sci U S A 1993, V90, P30 CAPLUS
 - (4) Benbrook, D; Nature 1988, V333, P669 CAPLUS
 - (5) Boehm, M; J Med Chem 1994, V37, P2930 CAPLUS
 - (6) Cacchi, S; Tetrahedron Lett 1985, V26, P1109 CAPLUS
 - (7) Crisp, G; J Org Chem 1992, V57, P6972 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2001 ACS

AN 1999:670110 CAPLUS

DN 131:286668

TI Preparation of 9-cis-retinoic acid analogs for increasing HDL levels

IN Epstein, Joseph William; Qing, Feng Ling; Birnberg, Gary Harold; Gilbert, Adam Matthew

PA American Cyanamid Company, USA

SO U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 359,141.

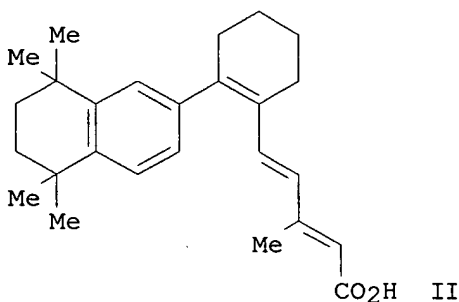
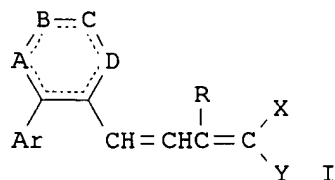
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5968908	A	19991019	US 1995-542146	19951114
	CA 2165374	AA	19960620	CA 1995-2165374	19951215
	AU 9540438	A1	19960627	AU 1995-40438	19951215
	AU 690772	B2	19980430		
	JP 08291094	A2	19961105	JP 1995-327423	19951215
	FI 9506086	A	19960620	FI 1995-6086	19951218
	EP 718285	A2	19960626	EP 1995-309171	19951218
	EP 718285	A3	19960807		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	HU 74007	A2	19961028	HU 1995-3627	19951218
	BR 9505938	A	19971223	BR 1995-5938	19951218
	CN 1176248	A	19980318	CN 1995-113178	19951218
	EP 997455	A1	20000503	EP 2000-101311	19951218
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
PRAI	US 1994-359141		19941219		
	US 1995-542146		19951114		
	EP 1995-309171		19951218		
OS	MARPAT 131:286668				
GI					



AB Novel analogs of 9-cis-retinoic acid I [Ar = (substituted) Ph, (substituted) tetrahydronaphthyl, (substituted) dihydroisobenzofuranyl; A, B, C = CH, CH₂, O, S; D = (CH)_m, (CH₂)_n; m = 0, 1; n = 0-2; R = H, Me, Et,

tert-Bu, CF₃; X = CH₂OH, CHO, (substituted) CO₂H, CN, CH₂CONH₂, tetrazol-5-yl; Y = H; XY = thiazolidinedionylidene], which are useful for the treatment and prevention of coronary artery disease and to protect against premature atherosclerosis by increasing HDL levels, are prepd. Thus, addn. of 2-bromo-5,6,7,8-tetrahydro-5,5,8,8-tetramethylnaphthalene to Et 2-trifluoromethanesulfonyloxycyclohexen-1-ylcarboxylate, followed by the addn. of Et 3-methyl-4-oxocrotonate gave the Et ester of II. II showed a potency of >5 times that of 9-cis-retinoic acid in its ability to bind to apolipoprotein.

IT **246518-53-6P**

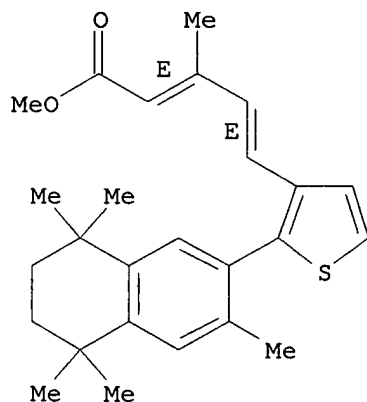
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 9-cis-retinoic acid analogs for increasing HDL levels)

RN 246518-53-6 CAPLUS

CN 2,4-Pentadienoic acid, 3-methyl-5-[2-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)-3-thienyl]-, methyl ester, (2E,4E)- (9CI)

(CA INDEX NAME)

Double bond geometry as shown.



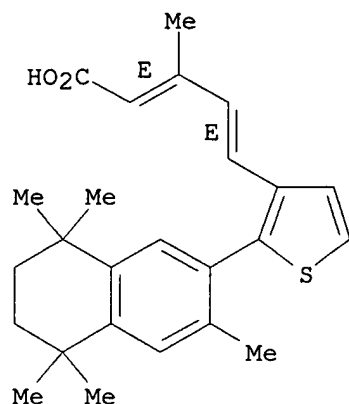
IT **246518-50-3P 246518-52-5P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 9-cis-retinoic acid analogs for increasing HDL levels)

RN 246518-50-3 CAPLUS

CN 2,4-Pentadienoic acid, 3-methyl-5-[2-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)-3-thienyl]-, (2E,4E)- (9CI) (CA INDEX NAME)

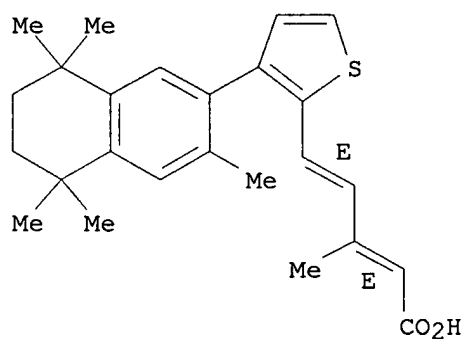
Double bond geometry as shown.



RN 246518-52-5 CAPLUS

CN 2,4-Pentadienoic acid, 3-methyl-5-[3-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)-2-thienyl]-, (2E,4E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RE.CNT 7

RE

(3) Anon; WO 9605165 1996 CAPLUS

(4) Gollnick, H; Retinoids:New Treads in Research and Therapy, Retinoid Symposium 1985, P445 CAPLUS

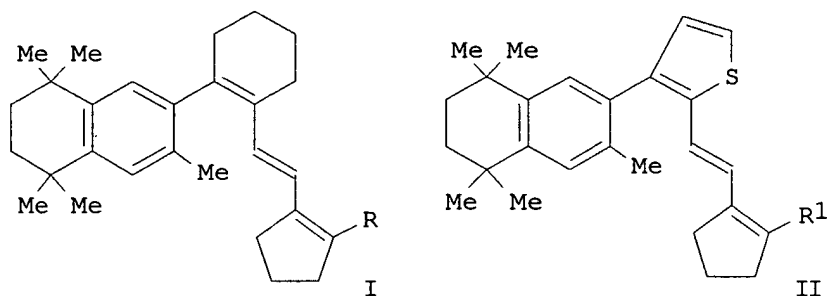
(5) Jong, L; J Med Chem 1993, V36, P2605 CAPLUS

(6) Rottman, J; Molecular and Cellular Biology 1991, V11(7), P3814 CAPLUS

(7) Zhang, X; Nature 1992, V358, P587 CAPLUS

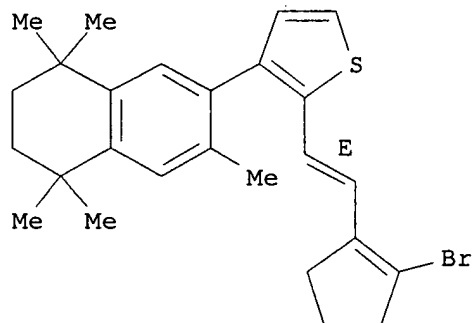
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2001 ACS
 AN 1997:749312 CAPLUS
 DN 128:34904
 TI A novel synthesis of 9,13-di-cis double bonds locked retinoids
 AU Qing, Feng-Ling; Yue, Xiang-Jun
 CS Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences,
 Shanghai, 200032, Peop. Rep. China
 SO Tetrahedron Lett. (1997), 38(46), 8067-8070
 CODEN: TELEAY; ISSN: 0040-4039
 PB Elsevier Science Ltd.
 DT Journal
 LA English
 OS CASREACT 128:34904
 GI



AB Synthesis of two retinoids in which the 9,13-dicis double bonds are locked
 in cycloalkene (I; R = CO₂H) or thiophene (II; R₁ = CO₂H) is described.
 The key step was carbonylation of vinyl bromides I (R = Br) and II (R₁ = Br) with carbon monoxide in the presence of Pd(PPh₃)₄.
 IT **199529-75-4P 199529-76-5P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (novel synthesis of 9,13-di-cis double bond-locked retinoids)
 RN 199529-75-4 CAPLUS
 CN Thiophene, 2-[(1E)-2-(2-bromo-1-cyclopenten-1-yl)ethenyl]-3-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)- (9CI) (CA INDEX NAME)

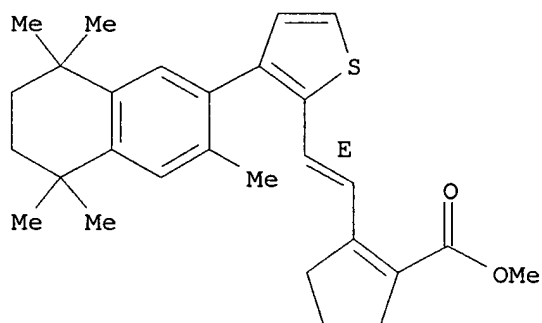
Double bond geometry as shown.



RN 199529-76-5 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[(1E)-2-[3-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)-2-thienyl]ethenyl]-, methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT 199529-63-0P

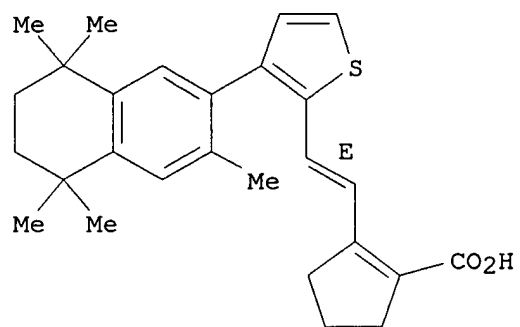
RL: SPN (Synthetic preparation); PREP (Preparation)
(novel synthesis of 9,13-di-cis double bond-locked retinoids)

RN 199529-63-0 CAPLUS

CN 1-Cyclopentene-1-carboxylic acid, 2-[(1E)-2-[3-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)-2-thienyl]ethenyl]- (9CI) (CA

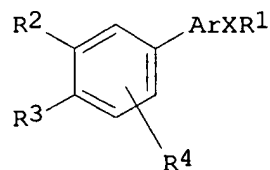
INDEX
NAME)

Double bond geometry as shown.



L14 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2001 ACS
 AN 1997:623162 CAPLUS
 DN 127:293119
 TI Preparation of bicyclic aromatic compounds
 IN Bernardon, Jean-Michel
 PA Centre International De Recherches Dermatologiques Galderma (C.I.R.D.
 Galder, Fr.; Bernardon, Jean-Michel
 SO PCT Int. Appl., 52 pp.
 CODEN: PIXXD2
 DT Patent
 LA French
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9733881	A1	19970918	WO 1997-FR391	19970305
	W:	AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	FR 2746101	A1	19970919	FR 1996-3235	19960314
	FR 2746101	B1	19980430		
	CA 2218766	AA	19970918	CA 1997-2218766	19970305
	AU 9720305	A1	19971001	AU 1997-20305	19970305
	AU 704753	B2	19990506		
	EP 832081	A1	19980401	EP 1997-908308	19970305
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
	CN 1190394	A	19980812	CN 1997-190489	19970305
	JP 10509987	T2	19980929	JP 1997-532318	19970305
	JP 2991502	B2	19991220		
	BR 9702200	A	19990720	BR 1997-2200	19970305
	NO 9705192	A	19980114	NO 1997-5192	19971112
	US 6147255	A	20001114	US 1998-952804	19980126
PRAI	FR 1996-3235		19960314		
	WO 1997-FR391		19970305		
OS	MARPAT 127:293119				
GI					



I

AB Novel bicyclic arom. compds. I [R1 = Me, CH2OR5, COR6; Ar = =

(un)substituted Ph, pyridyl, furyl, thienyl, pyrrolyl; X = CR8:CR9, C.tplbond.C; R2, R3 = H, alkyl, OR5, SR5; R2R3 = arom. ring; R5 = H, alkyl, acyl; R6 = H, alkyl, NR'R''; R8, R9 = H, alkyl] and their use in pharmaceutical compns. useful in treatment of dermatol. conditions (no data) or their use in cosmetic compns. (no data) are disclosed. E.g., reaction of 3-tert-butyl-4-methoxyphenylboronic acid and 4-bromo-2-thiophenecarboxaldehyde gave

4-(3-tert-butyl-4-methoxyphenyl)-2-thiophenecarboxaldehyde. The last was treated with tri-Et phosphonoacetate to give Et 4-(3-tert-butyl-4-methoxyphenyl)-2-thiopheneacrylate. The ester was converted to the corresponding acid.

IT 196960-63-1P 196960-64-2P 196960-65-3P

RL: BAC (Biological activity or effector, except adverse); BUU

(Biological

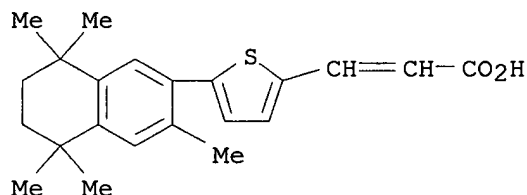
use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of bicyclic arom. compds.)

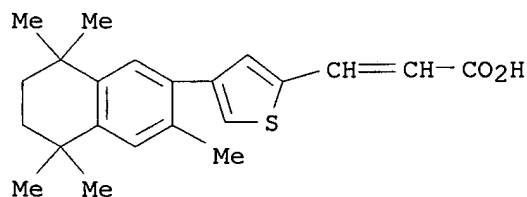
RN 196960-63-1 CAPLUS

CN 2-Propenoic acid, 3-[5-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)-2-thienyl]- (9CI) (CA INDEX NAME)



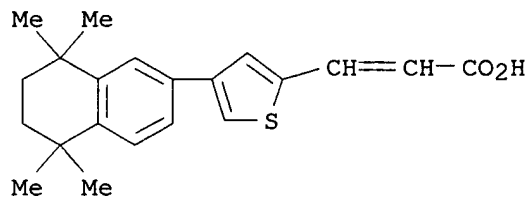
RN 196960-64-2 CAPLUS

CN 2-Propenoic acid, 3-[4-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)-2-thienyl]- (9CI) (CA INDEX NAME)



RN 196960-65-3 CAPLUS

CN 2-Propenoic acid, 3-[4-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)-2-thienyl]- (9CI) (CA INDEX NAME)



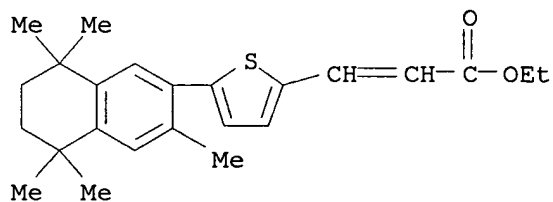
IT 196961-04-3P 196961-06-5P 196961-08-7P

196961-09-8P 196961-10-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of bicyclic arom. compds.)

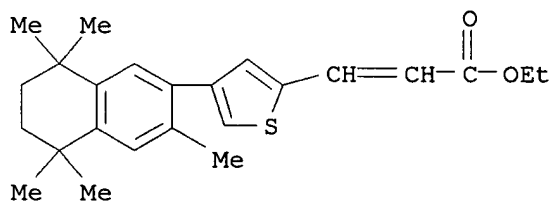
RN 196961-04-3 CAPLUS

CN 2-Propenoic acid, 3-[5-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)-2-thienyl]-, ethyl ester (9CI) (CA INDEX NAME)



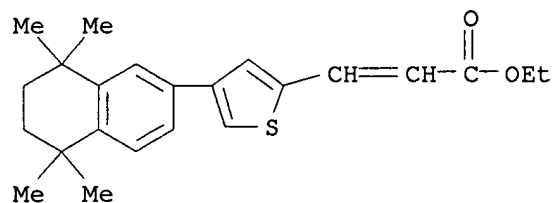
RN 196961-06-5 CAPLUS

CN 2-Propenoic acid, 3-[4-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)-2-thienyl]-, ethyl ester (9CI) (CA INDEX NAME)



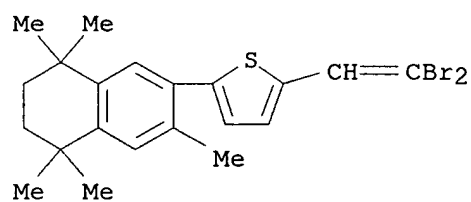
RN 196961-08-7 CAPLUS

CN 2-Propenoic acid, 3-[4-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)-2-thienyl]-, ethyl ester (9CI) (CA INDEX NAME)



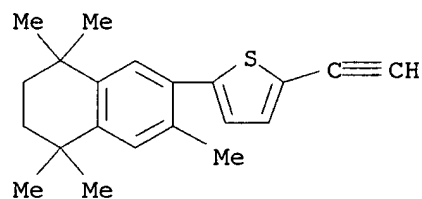
RN 196961-09-8 CAPLUS

CN Thiophene, 2-(2,2-dibromoethenyl)-5-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)- (9CI) (CA INDEX NAME)



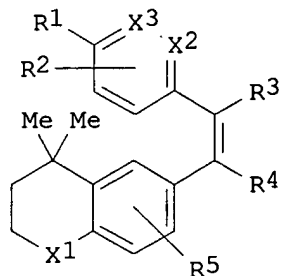
RN 196961-10-1 CAPLUS

CN Thiophene, 2-ethynyl-5-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)- (9CI) (CA INDEX NAME)

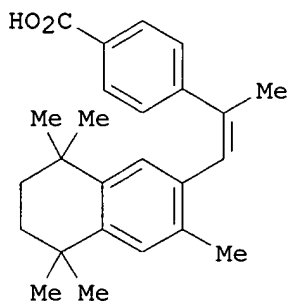


L14 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2001 ACS
 AN 1997:499165 CAPLUS
 DN 127:176578
 TI Preparation of aromatic polycyclic retinoid-type derivatives for making
 pharmaceutical and cosmetic compositions
 IN Leblond, Bertrand; Darro, Francis; Deyine, Abdallah; Sales-Sallans,
 Veronique; Duhamel, Pierre; Kiss, Robert; Schoofs, Alain-rene; Germain,
 Pierre; Pourrias, Bertrand; et al.
 PA Centre Europeen de Bioprospective - Ceb, Fr.; Leblond, Bertrand; Darro,
 Francis; Deyine, Abdallah; Sales-Sallans, Veronique; Duhamel, Pierre;
 Kiss, Robert; Schoofs, Alain-Rene; Germain, Pierre; Pourrias, Bertrand
 SO PCT Int. Appl., 192 pp.
 CODEN: PIXXD2
 DT Patent
 LA French
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9726237	A1	19970724	WO 1997-FR79	19970116
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2743560	A1	19970718	FR 1996-497	19960117
	FR 2743560	B1	19980403		
	CA 2243295	AA	19970724	CA 1997-2243295	19970116
	AU 9713145	A1	19970811	AU 1997-13145	19970116
	EP 879223	A1	19981125	EP 1997-900659	19970116
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000507208	T2	20000613	JP 1997-525493	19970116
PRAI	FR 1996-497		19960117		
	WO 1997-FR79		19970116		
OS	MARPAT 127:176578				
GI					



I



II

AB Polycyclic retinoid analogs I [X_1 = CMe₂, SO, SO₂; X_2 = X_3 = CH, O, NH, S, bond; R₁ = hydroxymethyl, OH, CHO, carboxyl, acyloxymethyl, SH, alkylthio, PO₃H₂, carbamoyl, tetrazolyl; R₂ = H, F, carboxy, alkyl, haloalkyl; R₃ = H, CF₃, F, alkyl, arylalkyl, alkyloxy, acyl; R₄ = H, aryl; R₅ = H, halogen, alkyl, arylalkyl, fluoroalkyl; R₅ = H, Me, Et] were prepd. for a variety of pharmaceutical and cosmetic uses including anticancer agents, non-insulin dependent diabetes agents, anti-inflammatories, and treatments

for skin disorders. Thus, retinoid analog II, as well as the corresponding E-isomer, were prepd. starting from 2,5-dimethyl-2,5-hexanediol and 4-cyanoacetophenone and were tested against ZR-75-1 and T-47D cancer cell lines for antitumor activity. Structure activity relationships for antitumor activity for analogs I was also presented.

IT 193954-96-0P, CB 92855 193977-01-4P, CB 07734

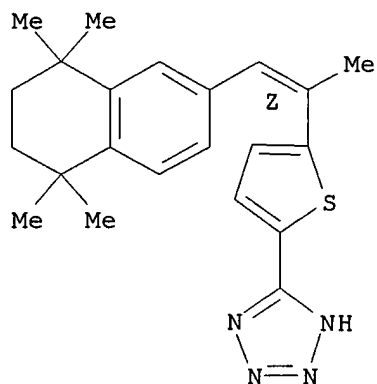
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of arom. polycyclic retinoid-type derivs. for making pharmaceutical and cosmetic compns.)

RN 193954-96-0 CAPLUS

CN 1H-Tetrazole, 5-[5-[1-methyl-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)ethenyl]-2-thienyl]-, (Z)- (9CI) (CA INDEX NAME)

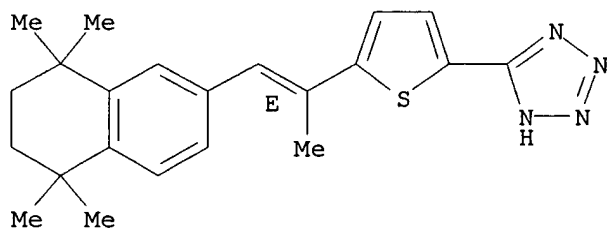
Double bond geometry as shown.



RN 193977-01-4 CAPLUS

CN 1H-Tetrazole, 5-[5-[1-methyl-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)ethenyl]-2-thienyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L14 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2001 ACS

AN 1996:365583 CAPLUS

DN 125:58784

TI Preparation of retinoic acid X receptor ligands

IN Klaus, Michael; Lovey, Allen John; Mohr, Peter; Rosenberger, Michael

PA F. Hoffmann-La Roche Ag, Switz.

SO PCT Int. Appl., 37 pp.

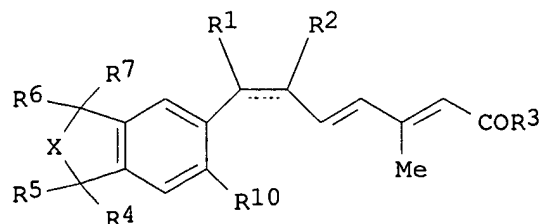
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9605165	A1	19960222	WO 1995-EP3021	19950729
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2196197	AA	19960222	CA 1995-2196197	19950729
	AU 9533821	A1	19960307	AU 1995-33821	19950729
	AU 696501	B2	19980910		
	EP 775103	A1	19970528	EP 1995-930430	19950729
	EP 775103	B1	19990609		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT,				
SE	CN 1152302	A	19970618	CN 1995-194064	19950729
	HU 76839	A2	19971128	HU 1997-356	19950729
	JP 09512830	T2	19971222	JP 1995-506962	19950729
	JP 2848964	B2	19990120		
	BR 9508985	A	19980106	BR 1995-8985	19950729
	AT 181052	E	19990615	AT 1995-930430	19950729
	ES 2133798	T3	19990916	ES 1995-930430	19950729
	PL 180048	B1	20001229	PL 1995-318557	19950729
	US 5801253	A	19980901	US 1997-776087	19970121
	FI 9700547	A	19970207	FI 1997-547	19970207
	NO 9700580	A	19970207	NO 1997-580	19970207
PRAI	EP 1994-112461		19940810		
	EP 1995-110460		19950705		
	WO 1995-EP3021		19950729		
OS	MARPAT 125:58784				
GI					



I

AB Title compds. I [R1 = lower alkyl; R2 = H, halo; or R1R2 = part of a carbocyclic ring; the dotted bond is part of the mesomeric system; or, when the dotted bond is absent, R1R2 = CH2 may form a cis-substituted cyclopropyl ring; R3 = OH, lower alkoxy; R4-R7 = H, lower alkyl; X = (CR8R9)_n where n = 1,2,3; R8, R9 = H, lower alkyl; R10 = H, alkyl, alkoxy]

and their pharmaceutically acceptable salts, useful for treatment of leukemia, are prepd. Thus, 6-bromo-1,1,4,4-tetramethyltetralin in THF was

treated with t-BuLi at -78.degree. for 30 min and then added to a mixt. prepd. from bis(triphenylphosphine)palladium(II) chloride and diisobutylaluminum hydride in THF, the resulting mixt. was treated with

Et 2-iodobenzoate and then stirred overnight at room temp. to give, after treatment with 2N HCl,

2-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)benzoic acid Et ester. Hydride redn. of this gave the corresponding alc., which was oxidized to the corresponding aldehyde, whose reaction with 4-(diethoxyphosphinyl)-3-methylcrotonic acid Et ester in pentane-THF contg. NaH gave, after sapon., the title compd. (2E,4E)-3-methyl-5-[2-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)phenyl]penta-2,4-dienoic acid. Pharmaceutical compns. contg. I are described.

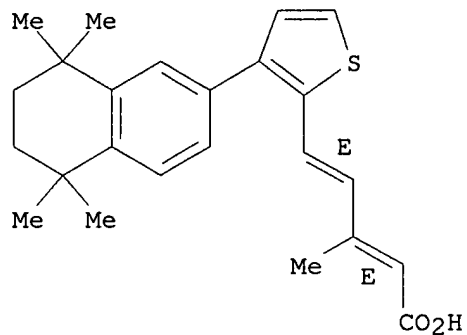
IT 173104-28-4P 177740-99-7P 177741-00-3P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of retinoic acid X receptor ligands)

RN 173104-28-4 CAPLUS

CN 2,4-Pentadienoic acid, 3-methyl-5-[3-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)-2-thienyl]-, (E,E)- (9CI) (CA INDEX NAME)

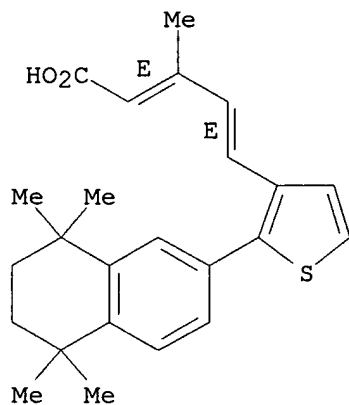
Double bond geometry as shown.



RN 177740-99-7 CAPLUS

CN 2,4-Pentadienoic acid, 3-methyl-5-[2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)-3-thienyl]-, (E,E)- (9CI) (CA INDEX NAME)

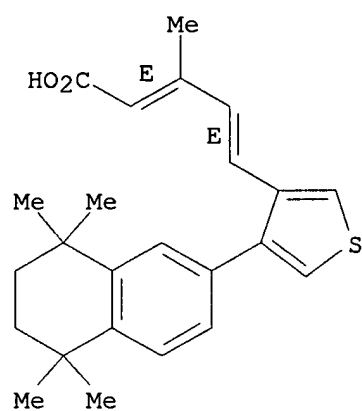
Double bond geometry as shown.



RN 177741-00-3 CAPLUS

CN 2,4-Pentadienoic acid, 3-methyl-5-[4-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)-3-thienyl]-, (E,E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L14 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2001 ACS

AN 1996:11680 CAPLUS

DN 124:105640

TI Enhancement of HL-60 differentiation by a new class of retinoids with selective activity in retinoid X receptor

AU Apfel, Christian M.; Kamber, Markus; Klaus, Michael; Mohr, Peter; Keidel, Siegfried; LeMotte, Peter K.

CS Dep. Dermatol., F. Hoffmann-LaRoche, Basel, CH-4002, Switz.

SO J. Biol. Chem. (1995), 270(51), 30765-72

CODEN: JBCHA3; ISSN: 0021-9258

DT Journal

LA English

AB Cellular responsiveness to retinoic acid and its metabolites is conferred through two distinct families of receptors: the retinoic acid receptors (RARs) and the retinoid X receptors (RXRs). Herein, the authors report on

the identification and characterization of several conformationally restricted retinoids, which selectively bind and activate RX receptors. Under the influence of retinoids, HL-60 myelocytic leukemia cells differentiate into granulocytes. This effect is mediated by RAR.alpha., as has been demonstrated through the use of a selective RAR.alpha. antagonist (Apfel, C., Bauer, F., Crettaz, M., Forni, L., Kamber, M., Kaufmann, F., LeMotte, P., Pirson, W., and Klaus, M. (1992) Proc. Natl. Acad. Sci. U. S. A. 89, 7129-7133). Here, the authors show that conformationally restricted RXR-specific retinoids, at doses that are per se inactive, are able to potentiate by up to one order of magnitude the pro-differentiating effects of all-trans retinoic acid and an RAR.alpha.-selective synthetic retinoid. The authors also present evidence that these RXR-selective ligands are able to bind to a DNA RXR.cntdot.RAR heterodimer complex. This finding demonstrates that agonists for RARs and RXRs can synergistically promote HL-60 differentiation, which could be mediated through a heterodimer of these receptors.

IT 173104-28-4

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(enhancement of HL-60 differentiation by a new class of retinoids with selective activity at the retinoid X receptor)

RN 173104-28-4 CAPLUS

CN 2,4-Pentadienoic acid, 3-methyl-5-[3-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)-2-thienyl]-, (E,E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

